UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,279	11/24/2003	Richard A. Hopkins	21486-027DIV	6395

7590 07/13/2006

MINTZ, LEVIN, COHN, FERRIS,
GLOVSKY and POPEO, P.C.
One Financial Center
Boston, MA 02111

EXAMINER	
BLANCO, JAVIER G	
ART UNIT	**PAPER NUMBER**
3738	

DATE MAILED: 07/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/722,279	HOPKINS ET AL.	
	Examiner	Art Unit	
	Javier G. Blanco	3738	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-24 and 26-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24 and 26-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicants' addition of dependent claim 52 in the reply filed on April 28, 2006 is acknowledged.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 21-24 and 26-52 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Goldstein et al. (US 5,899,937 A) or, in the alternative, under 35 U.S.C. 103(a) as obvious over Goldstein et al. (US 5,899,937 A) in view of Bishopric et al. (US 5,855,620 A) and Vacanti et al. (US 6,348,069 B1).

Goldstein et al. disclose a method of manufacturing a bioprosthetic heart valve comprising:

(i) Providing an acellular or decellularized porcine valve (see column 1, lines 58-62; column 5, lines 24-26);

(ii) Seeding said acellular or decellularized porcine valve with isolated fibroblasts (i.e., dermal myofibroblasts; see column 1, line 61 to column 2, line 4; column 3, lines 11-13; column 6, lines 44-63; column 13, lines 7-11 and lines 15-24) wherein the myofibroblasts produce at least two-fold more type I collagen compared to type III collagen (see Abstract; column 1, lines 58-67;

column 2, lines 1-67; column 6, lines 44-62; column 13, lines 7-11 and lines 20-24; column 14, line 65; see entire document); and,

(iii) Culturing said myofibroblasts under pulsatile flow conditions (see Abstract; see column 2, lines 50-53; column 3, lines 10-13; column 7, lines 53-67; column 9, lines 21-25; column 14, lines 27-37).

a. Goldstein et al. teach: "endothelial cells do not seem to be necessarily to prevent thrombus formation" (see column 6, lines 45-57). This is not an exclusive negative teaching. Further in Goldstein et al. specification, Goldstein et al. disclose known background directed to benefits using endothelial cells (see column 14, lines 43-56). While Goldstein does not deem it necessary (with respect to prevention of thrombosis) to use endothelial cells, this is not an inclusive bar against using endothelial cells in forming heart valves.

b. Bishopric et al. '620 teach that endothelial cells along with myofibroblasts (as well as other cell types) may be seeded on an acellularized matrix in vitro in order to form heart valves (see column 5, lines 33-36; column 6, lines 5-7; column 7, lines 50-67). Vacanti et al. '069 likewise teach that endothelial cells along with myofibroblasts (as well as other cell types) may be seeded on an acellularized matrix in vitro in order to form heart valves (see column 6, lines 25-35 and lines 40-43; column 7, line 60 to column 8, line 13). Vacanti et al. further teach that those cells can be "normal or genetically engineered to provide additional or normal function" (see column 6, lines 35-39). Looking to Applicant's specification, the endothelial cells and/or secretory cell are referred to as an option (i.e., no criticality), as disclosed at page 4, lines 14-16, and page 8, lines 5-6. Absence any showing of criticality, it was well known in the art (Bishopric et al. '620,

and Vacanti et al. '069) to use more than one type of cell population in order to form heart valves.

Response to Arguments

4. Applicants' arguments filed April 28, 2006 have been fully considered but they are not persuasive.

a. The Applicants argue that Goldstein et al. '937 does not disclose "isolated" cells. The Examiner respectfully disagrees. By reading the disclosure of Goldstein et al. '937 a person skilled in the art will clearly understand that repopulation/seeding of the acellular matrix involves using a single-type population which is substantially free of any other cell types or compositions. Column 1, line 61 to column 2, line 4; column 3, lines 11-13; column 6, lines 44-63; and column 13, lines 7-11 and lines 15-24 clearly shows that Goldstein et al. '937 is using isolated cells. Further, the Applicants' RESPONSE, at page 8 (see last two paragraphs), admits that Goldstein et al. '937 uses isolated cells. The Applicants also argue that Goldstein et al. '937 does not disclose myofibroblast as "encompassed by the claim term". The Examiner respectfully disagrees. As admitted by the Applicants, dermal or vascular fibroblasts acquire myofibroblast phenotype in the presence of tissue culture conditions and/or cell signaling factors (see specification at page 9, lines 10-18). These "tissue culture conditions and/or cell signaling factors" are also used in the invention of Goldstein et al. '937, and are already known in the art. Goldstein et al. '937 teach that their bioprosthetic heart valves "attempt to mimic, as closely as possible the distribution of cells and the expression of cell activities found in a native leaflet that

are considered important for long-term leaflet durability" (see column 6, lines 47-52; column 14, lines 31-38).

b. The Applicant argues that Bishopric et al. '620 "fails to isolate and rigorously characterize each specific cell type used for seeding". The Examiner respectfully disagrees. As previously indicated (see rejection above), Bishopric et al. '620 teach that endothelial cells along with myofibroblasts (as well as other cell types) may be seeded on an acellularized matrix in vitro in order to form heart valves (see column 5, lines 33-36; column 6, lines 5-7; column 7, lines 50-67). Column 5, at lines 33-36, clearly indicates repopulation/seeding of the acellular matrix with fibroblasts and endothelial cells. Column 7, at lines 51-63, clearly indicate different cell types (e.g., myofibroblasts) that may be used to repopulate/seed the acellular matrix. Looking at the claim language (e.g., dependent claim 23, among others), it is noted that the claim language is open (i.e., "comprising") to the use of other cell types, which is the same teaching of Bishopric et al. '620.

c. The Applicant argues that Vacanti et al. '069 "fails to describe or suggest a population of isolated myofibroblasts as required by the claims". The Examiner respectfully disagrees. Vacanti et al. '069 teach that endothelial cells along with myofibroblasts (as well as other cell types) may be seeded on an acellularized matrix in vitro in order to form heart valves (see column 6, lines 25-35 and lines 40-43; column 7, line 60 to column 8, line 13). Vacanti et al. '069 clearly disclose dissociated (i.e., isolated) cell types (e.g., fibromyoblasts/myofibroblasts) in column 6, lines 25-34, and column 7, line 60 to column 8, line 17. Looking at the claim language (e.g., dependent claim 23, among others), it is noted that the claim language is open (i.e., "comprising") to the use of other cell types, which is the same teaching of Vacanti et al. '069.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Javier G. Blanco whose telephone number is 571-272-4747. The examiner can normally be reached on M-F (9:30 a.m.-7:00 p.m.), first Friday of the bi-week off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Corrine McDermott can be reached on (571) 272-4754. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306 for regular communications and After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0858.

JGB July 7, 2006

David H. Willse
Primary Examiner